

Appl. No. 09/508,510
Amdt. Dated October 25, 2004
Reply to Office Action of May 25, 2004

REMARKS

Claims 1-9, 11-14, 17-23, 25-29, 32, and 33 were pending in the instant application. This Amendment follows and makes of record a personal interview held October 14, 2004, in which Examiner Andres, Applicants' undersigned attorney, Patrick T. Skacel, and Applicants' representatives Dr. Josef Brzoska, and Mr. Thomas Siklosi were present. The courtesies extended by the Examiner at the interview are greatly appreciated by all.

By this Amendment, Applicants have canceled claims 1, 2, 4-8, 17, 21-23, and 25-26 without prejudice to the presentation of the subject matter contained therein in a future continuation or divisional application. Applicants have amended claim 3 to incorporate therein subject matter from claim 17 as discussed at the interview. Claim 11 has been amended for clarity, with specific support for the amendment being found, *inter alia*, at page 9, lines 9-10 in the specification. Claims 13 and 14 have been amended to change their dependencies to claim 3. Applicants have added new claims 34-38. New independent claim 35 replaces, and incorporates subject matter from, now canceled claims 25 and 26. New claims 37-38 provide concentrations for the interferon- β in the recited formulation, support for which can be found, *inter alia*, at page 13. Support for all of the amendments and new claims can be found throughout the specification and claims as originally filed. The present Amendment does not introduce any new matter, and thus, its entry is requested. Upon entry of the present Amendment, claims 3, 9, 11-14, 18-20, 27-29, and 32-38 will be pending and under examination. Applicants request early allowance of the present application.

The May 25, 2004 Office Action

Information Disclosure Statement

The Examiner indicated that the Information Disclosure Statement filed October 7, 2003 has been considered in full.

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Claim rejections withdrawn

The Examiner withdrew the rejection of claims 1-14, 17-23, and 26-31 under 35 U.S.C. §112, second paragraph in response to Applicants' previous Amendment.

In response, Applicants acknowledge and appreciate the withdrawal of this rejection.

Examiner's rejection/objection under 35 U.S.C. §132 and 35 U.S.C. §112, first paragraph

The Examiner objected to Applicants' previous Amendment under 35 U.S.C. §132, asserting that the Amendment "introduces new matter into the disclosure." according to the Examiner, the added material not supported by the original disclosure is the limitation of "less than 12×10^6 U/ml." The Examiner also rejected claims 1, 2, 4-8, 13, 14, and 21-23 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement due to the same recitation in the claims.

In response, Applicants first note that 35 U.S.C. §132 is a proper ground for rejection only when new matter has been added to the disclosure, not the claims, and thus, that section is not applicable here. Nevertheless, without conceding the correctness of the Examiner's position with respect to section 112, but to advance prosecution of the subject application, Applicants have canceled claims 1, 2, 4-8, and 21-23 without prejudice. Applicants furthermore have amended claims 13 and 14 to change their dependencies to claim 3. Applicants believe these claim cancellations and amendments fully overcome the Examiner's concerns. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the objection under 35 U.S.C. §132 and the rejection under 35 U.S.C. §112, first paragraph.

Examiner's rejections under 35 U.S.C. §112, second paragraph

The Examiner rejected claim 11 under 35 U.S.C. §112, second paragraph, as being indefinite in its recitation of the phrase "the active ingredient is free from human or animal polypeptides." The Examiner pointed out that the active ingredient itself, IFN- β , is an animal polypeptide. Moreover, the Examiner noted that because humans are animals, the use of the term

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“human or animal” is also indefinite.

In response, without conceding the correctness of the Examiner’s position, but to advance prosecution of the subject application, Applicants have amended claim 11 to recite the “formulation according to Claim 3, wherein the formulation, apart from the active ingredient, is free from animal polypeptides.” In light of this amendment, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claim 11 under 35 U.S.C. §112, second paragraph.

The Examiner also rejected claims 1, 2, 4-9, 13, 14, 21-23, and 26 under 35 U.S.C. §112, second paragraph, in their recitation of “U”. Specifically, the Examiner indicated that there has been some confusion and inconsistency in the use of the terms “IU”, “U”, and “unit” during prosecution of the case.

In response, Applicants point out that the specification, at page 13, lines 31-32, defines “MU/ml” as “10⁶ IU/ml”. Page 12, first paragraph, specifically refers to formulations that preferably exist in unit doses of 1 to 25 MU IFN-β. Therefore, the terminology “1 to 25 x 10⁶ IU of interferon-β,” as it appears in claim 29, is clear as written and consistent with the specification. Claims 1, 2, 4-8, and 21-23 have been canceled, and claims 13 and 14 have been amended, as discussed above. Accordingly, Applicants have fully overcome the Examiner’s rejection and respectfully request that the rejection be withdrawn.

Examiner’s Rejection under 35 U.S.C. 102(b) and 35 U.S.C. 102/103

The Examiner has recast the previous rejection of claims 1, 2, 4-8, 13, 14, and 21-23 under 35 U.S.C. §102(b), over EP 0 529 300 B1, as a combination anticipation/obviousness rejection under 35 U.S.C. §102/103, pointing out that such a combination rejection is permitted when it is unclear if the cited reference teaches the claimed range with “sufficient specificity.” Applicants recognize that in such a rejection, the Examiner is required to provide reasons for anticipation as well as indicate a statement of motivation regarding obviousness.

Applicants note that the Examiner’s confusion concerning the dosage terminology

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reflected in the indefiniteness rejection above has led her to assert that it is unclear what concentrations are being claimed in the present application. In the rejection itself, the Examiner essentially repeated the previous assertion that “consisting essentially of” as recited in the claims does not exclude the presence of agents such as PVP, which is referred to in the EP 0 529 300 B1 document as an alternative filler to HSA. The Examiner referred to Example 4 in support of this rejection. The Examiner has acknowledged that Example 3 recites only formulations that contain “certain concentrations” of IFN- β . All of these concentrations are outside the claimed ranges. The Examiner asserted, however, that there is nothing in the remainder of the reference that would exclude any ranges from these particular preparations. The Examiner concluded that there is nothing in the rejected claims that distinguishes the claimed compositions from the teachings of the EP 0 529 300 B1 reference. Moreover, the Examiner asserted that even if a distinction existed between the claimed concentrations and those used in the reference, it would be obvious to use the lower concentrations of IFN- β claimed in the compositions of the cited reference, because in the Examiner’s view, the reference teaches no lower concentration limits in liquid solutions, and appears to teach a range of physiologically acceptable concentrations that include lower concentrations than those claimed.

In response, without conceding the correctness of the Examiner’s position, but to expedite allowance of the subject application, Applicants have canceled claims 1, 2, 4-8, and 21-23 without prejudice, and amended claims 13 and 14 (as noted above), thereby rendering the Examiner’s rejection moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. 102(b)/103.

Examiner’s Rejection under 35 U.S.C. 103(a)

The Examiner maintained the rejection of claims 3, 9, 11, 12, 17-20, and 25-29 under 35 U.S.C. §103, as allegedly being obvious over the EP 0529300 reference and the Patel patent of record (U.S. Patent No. 5,358,708). The Examiner has asserted that Patel’s use of methionine to stabilize interferon- α formulations would have motivated one of skill in the art to use such a

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stabilizer to stabilize interferon-β formulations, such as those claimed by Applicants.

Applicants do not agree with the Examiner's position. Nevertheless, to expedite allowance of the subject application, but without conceding the correctness of the Examiner's position, Applicants have amended claim 3 to recite a concentration range of methionine of 0.1 to 4 mmol/l. As Applicants pointed out during the interview with the Examiner, and as the Examiner acknowledged, the Patel patent teaches using significantly higher concentrations in its formulations than those which are used in the instant application. Patel clearly provides no motivation to use methionine in the concentrations of the Applicants' claims, as amended. Therefore, Applicants believe the rejection has been fully overcome. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §103.

The October 14, 2004 Interview

In the October 14, 2004 interview, the obviousness rejection of claim 3 and those depending therefrom was discussed, with particular focus on the Patel reference. Applicants pointed out that the Patel reference teaches neither interferon-β formulations, nor stability as it relates to biological activity. Rather, Patel refers to an interferon-α, which has different characteristics than interferon-β, and to chemical stability, which is unrelated to biological activity. The issue of whether, if the claimed combination were obvious over that taught in Patel, biological stability was an inherent characteristic of such a formulation was raised by the Examiner.

Applicants demonstrated, through a series of conversion calculations, that the concentration of methionine taught in the Applicants' formulations is significantly less than that referred to in Patel, and that Patel clearly shows no motivation to use such lower levels. The Examiner acknowledged this clear difference in concentration levels. As discussed above, to expedite allowance, Applicants have now introduced such methionine concentrations into the claims.

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In view of the above remarks and amendments, Applicants believe that the Examiner's rejections set forth in the May 25, 2004 Office Action have been fully overcome and that the present application is in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,



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